

## WHAT IS CLAIMED IS:

1                    1.     A method for modulating expression of a mammalian SREBP-1 gene,  
2     the method comprising administering a modulator compound that promotes or inhibits  
3     LXR $\alpha$ -mediated expression of the SREBP-1 gene to a cell that comprises an SREBP-1 gene  
4     and an LXR $\alpha$  polypeptide.

1                    2.     The method of claim 1, wherein the modulator compound is an agonist  
2     of LXR $\alpha$  and promotes LXR $\alpha$ -mediated expression of the SREBP-1 gene.

1                    3.     The method of claim 1, wherein the modulator compound promotes or  
2     inhibits LXR $\alpha$ -mediated expression of the SREBP-1c transcript.

1                    4.     The method of claim 2, wherein the modulator compound is 24,25-  
2     epoxycholesterol.

1                    5.     The method of claim 1, wherein the modulator compound is an  
2     antagonist of LXR $\alpha$  and inhibits LXR $\alpha$ -mediated expression of the SREBP-1 gene.

1                    6.     The method of claim 5, wherein the cell further comprises one or more  
2     genes that encode an enzyme involved in fatty acid and triglyceride metabolism and  
3     contacting the cell with the modulator compound inhibits expression of one or more of the  
4     genes that encode an enzyme involved in fatty acid and triglyceride metabolism.

1                    7.     The method of claim 1, wherein the enzyme involved in fatty acid and  
2     triglyceride metabolism is selected from the group consisting of fatty acid synthase, acetyl  
3     CoA carboxylase, steroyl CoA desaturase, and lipoprotein lipase.

1                    8.     The method of claim 1, wherein the cell is in a mammal.

1                    9.     The method of claim 8, wherein the mammal is a human.

1                    10.    The method of claim 8, wherein the modulator compound is an  
2     antagonist of LXR $\alpha$  and triglyceride levels in the mammal are reduced.

1                    11.    The method of claim 8, wherein the modulator compound is an  
2     antagonist of LXR $\alpha$  and insulin levels in the mammal are reduced.

12. A method of modulating triglyceride levels in a mammal, the method comprising administering to the mammal an effective amount of a modulator compound that inhibits LXR $\alpha$ -mediated expression of an SREBP-1 gene in cells of the mammal.

13. The method of claim 12, wherein mammal is a human.

14. A method of prescreening to identify a candidate therapeutic agent that modulates SREBP-1 expression in a mammal, the method comprising:

providing a reaction mixture which comprises:

a polypeptide that comprises an LXR $\alpha$  ligand binding domain (LBD);

a ligand for LXR $\alpha$ ; and

a test compound; and

determining whether the amount of LXR $\alpha$  ligand that binds to the LBD is increased or decreased in the presence of the test compound relative to the amount of ligand that binds to the LBD in the absence of the test compound;

wherein a test compound that causes an increase or decrease in the amount of LXR $\alpha$  ligand binding to the LBD is a candidate therapeutic agent for modulation of SREBP-1 expression in a mammal.

15. The method of claim 15, wherein the method further comprises administering the candidate therapeutic agent to a cell which comprises a SREBP-1 gene to determine whether the candidate therapeutic agent modulates expression of the SREBP-1 gene in the cell, and/or expression of a gene that is regulated by SREBP-1.

16. The method of claim 15, wherein the gene that is regulated by SREBP-1 encodes an enzyme involved in fatty acid and/or triglyceride metabolism.

17. The method of claim 16, wherein the enzyme involved in fatty acid and/or triglyceride metabolism is selected from the group consisting of fatty acid synthase, acetyl CoA carboxylase, steroyl CoA desaturase, and lipoprotein lipase.

18. The method of claim 15, wherein the gene that is regulated by SREBP-1 encodes an enzyme involved in adipocyte differentiation.

- 1 19. The method of claim 15, wherein the cell is in a mammal.
- 1 20. The method of claim 14, wherein the ligand for LXR $\alpha$  is a peptide  
2 sensor.
- 1 21. The method of claim 20, wherein the peptide sensor is derived from an  
2 RXR.
- 1 22. The method of claim 20, wherein the peptide sensor is derived from a  
2 coactivator or corepressor.
- 1 23. The method of claim 22, wherein the coactivator is SRC-1 or NCOR.
- 1 24. The method of claim 20, wherein the peptide sensor is derived from a  
2 coactivator and comprises an amino acid sequence LXXLL, where X is any amino acid.
- 1 25. The method of claim 20, wherein the peptide sensor is derived from a  
2 corepressor and comprises an amino acid sequence IXXII, where X is any amino acid.
- 1 26. The method of claim 20, wherein the peptide sensor comprises a  
2 detectable label.
- 1 27. The method of claim 14, wherein the ligand for LXR $\alpha$  is a coactivator  
2 or corepressor.
- 1 28. The method of claim 14, wherein the ligand for LXR $\alpha$  is an oxysterol.
- 1 29. The method of claim 28, wherein the oxysterol is 24,25-  
2 epoxycholesterol.
- 1 30. The method of claim 14, wherein the amount of binding is determined  
2 using a FRET assay.
- 1 31. The method of claim 14, wherein the amount of binding is determined  
2 using a fluorescence polarization assay.
- 1 32. The method of claim 14, wherein the amount of binding is determined  
2 using ELISA.

1 33. The method of claim 14, wherein the amount of binding is determined  
2 using a direct binding assay.

1 34. A method for ameliorating a condition associated with abnormal  
2 SREBP-1 expression in a mammal, the method comprising administering to the mammal a  
3 therapeutically effective amount of a LXR $\alpha$  antagonist.

1 35. The method of claim 34, wherein the condition associated with  
2 abnormal SREBP-1 expression is hypertriglyceridemia.

1 36. The method of claim 34, wherein the condition associated with  
2 abnormal SREBP-1 expression is lipodystrophy.

1 37. The method of claim 36, wherein the lipodystrophy is congenital  
2 generalized lipodystrophy.

1 38. The method of claim 34, wherein the condition associated with  
2 abnormal SREBP-1 expression is insulin resistance.

1 39. The method of claim 34, wherein the condition associated with  
2 abnormal SREBP-1 expression is an elevated plasma insulin level.

1 40. The method of claim 34, wherein the condition associated with  
2 abnormal SREBP-1 expression is hyperglycemia and/or diabetes mellitus.

1 41. The method of claim 34, wherein the condition associated with  
2 abnormal SREBP-1 expression is a syndrome associated with treatment of AIDS by  
3 administration of an HIV protease inhibitor, which syndrome is characterized by one or more  
4 of lipodystrophy, insulin resistance and hyperlipidemia.